PATENT
Attorney Docket No.: A-63761-7/RFT/RMS/RMK

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	)	Examiner: Unknown
	)	
Kayyem *et al.*	)	Group Art Unit: Unknown
	)	
Serial No. Not Assigned	)	
	)	
Filed: June 12, 1997	)	
	)	
For: *Electrodes Linked Via Conductive Oligomers to Nucleic Acids*	)	

"EXPRESS MAIL" MAILING LABEL
NUMBER EL 890 441385 US
DATE OF DEPOSIT February 20, 2002
I HEREBY CERTIFY THAT THIS PAPER OR FEE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE "EXPRESS MAIL POST OFFICE TO ADDRESSEE" SERVICE UNDER 37 CFR 1.10 ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO: BOX PATENT APPLICATION FEE, ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, DC 20231.

TYPED NAME Darryl Krinen
SIGNED

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

Prior to examination, please amend the above referenced application as follows. The Commissioner is authorized to charge any fees, including extension fees or other relief which may be required, or credit any overpayment to Deposit Account No. 06-1300 (Our Order No. A-63761-7/RFT/RMS).

In the Claims:

Please cancel claim 1.

Please add the following claims:

47. A composition comprising:

a) an electrode comprising a self-assembled monolayer comprising nucleic acid probes attached to said electrode with a spacer; and

b) a hybridization indicator.

48. A composition according to claim 47 wherein said hybridization indicator is an intercalator.

49. A composition according to claim 47 wherein said hybridization indicator is methylene blue.

50. A composition according to claim 47 further comprising a target nucleic acid hybridized to said probe to form a hybridization complex, wherein said hybridization indicator is associated with said hybridization complex.

51. A composition comprising a first single stranded nucleic acid hybridized to a second single stranded nucleic acid forming a hybridization complex, said hybridization complex comprising one or more electron donor moieties and one or more electron acceptor moieties, wherein one of said electron donor or acceptor moieties is an electrode and the other electron donor or acceptor moiety is an intercalator.

52. A composition according to claim 47 further comprising a co-reductant.

53. A composition according to claim 47 wherein said nucleic acid probe is a single stranded nucleic acid.

54. A composition according to claim 47 wherein said nucleic acid probe comprises a double stranded portion.

55. A composition according to claim 47 further comprising a soluble electron source.

56. A composition according to claim 55 where said soluble electron source comprises ferricyanide.

57. A composition according to claim 47 wherein said spacer is a conductive oligomer.

58. A composition according to claim 47 wherein said spacer is an insulator.

59. A composition according to claim 58 wherein said insulator comprises $(CH_2)_6$.

60. A composition according to claim 47 wherein said self-assembled monolayer further comprises passivation agents.

61. A composition according to claim 60 wherein said passivation agents are insulators.

62. A composition comprising:

a) a hybridization indicator; and

b) an array of electrodes, each comprising

i) a self-assembled monolayer;

ii) a nucleic acid probe attached to said electrode with a spacer.

63. A composition according to claim 62 wherein said hybridization indicator is an intercalator.

64. A composition according to claim 62 wherein said hybridization indicator is methylene blue.

65. A composition according to claim 62 further comprising a target nucleic acid hybridized to said probe to form a hybridization complex, wherein said hybridization indicator is associated with said hybridization complex.

66. A composition according to claim 62 further comprising a co-reductant.

67. A composition according to claim 62 wherein said nucleic acid probe is a single stranded nucleic acid.

68. A composition according to claim 62 wherein said nucleic acid probe comprises a double stranded portion.

69. A composition according to claim 62 further comprising a soluble electron source.

70. A composition according to claim 69 where said soluble electron source comprises ferricyanide.

71. A composition according to claim 62 wherein said spacer is a conductive oligomer.

72. A composition according to claim 62 wherein said spacer is an insulator.

73. A composition according to claim 72 wherein said insulator comprises $(CH_2)_6$.

74. A composition according to claim 62 wherein said self-assembled monolayer further comprises passivation agents.

75. A composition according to claim 74 wherein said passivation agents are insulators.

76. A method of detecting a target sequence in a sample comprising:

a) providing a composition comprising:

i) a self-assembled monolayer; and

ii) a nucleic acid probe attached to said electrode with a spacer;

b) hybridizing said target sequence to said nucleic acid probe to form a hybridization complex;

c) providing a hybridization indicator that associates with said complex; and

d) detecting electron transfer between said hybridization indicator and said electrode as an indication of the presence of said target sequence.

77. A method according to claim 76 wherein said spacer is a conductive oligomer.

78. A method according to claim 76 wherein said spacer is an insulator.

79. A method according to claim 78 wherein said insulator comprises $(CH_2)_6$.

80. A method according to claim 76 wherein said hybridization indicator is an intercalator.

81 A method according to claim 76 wherein said hybridization indicator is methylene blue.

82. A method according to claim 76 wherein said detecting is done using chronocoulometry.

83. A composition according to claim 76 further comprising a target nucleic acid hybridized to said probe to form a hybridization complex, wherein said hybridization indicator is associated with said hybridization complex.

84. A method according to claim 76 further comprising providing a co-reductant.

85. A method according to claim 76 wherein said nucleic acid probe comprises single stranded nucleic acid.

86. A method according to claim 76 wherein said nucleic acid probe comprises a double stranded portion.

87. A method according to claim 76 further comprising providing a soluble electron source.

88. A method according to claim 87 wherein said soluble electron source comprises ferricyanide.

89. A method according to claim 76 wherein said self-assembled monolayer further comprises passivation agents.

90. A method according to claim 89 wherein said passivation agents are insulators.

91. A method of detecting a mutation in a target sequence comprising:

a) providing a composition comprising:

i) a self-assembled monolayer; and

ii) a nucleic acid probe attached to said electrode with a spacer, wherein said probe comprises a base substitution as compared to said target sequence;

b) hybridizing said target sequence to said nucleic acid probe to form a hybridization complex;

c) providing a hybridization indicator that preferentially binds to perfectly complementary hybridization complexes over hybridization complexes that comprise a mismatch; and

d) detecting electron transfer between said hybridization indicator and said electrode as an indication of the presence of a mutation in said target sequence.

92. A method according to claim 91 wherein said hybridization indicator is an intercalator.

93. A method according to claim 91 wherein said hybridization indicator is methylene blue.

94. A method according to claim 91 further comprising a target nucleic acid hybridized to said probe to form a hybridization complex, wherein said hybridization indicator is associated with said hybridization complex.

95. A method according to claim 91 further comprising providing a co-reductant.

96. A method according to claim 91 wherein said nucleic acid probe is a single stranded nucleic acid.

97. A method according to claim 91 wherein said nucleic acid probe comprises a double stranded portion.

98. A method according to claim 91 further comprising providing a soluble electron source.

99. A method according to claim 98 wherein said soluble electron source comprises ferricyanide.

100. A method according to claim 91 wherein said spacer is a conductive oligomer.

101. A method according to claim 91 wherein said spacer is an insulator.

102. A method according to claim 101 wherein said insulator comprises $(CH_2)_6$.

103. A method according to claim 91 wherein said self-assembled monolayer further comprises passivation agents.

104. A method according to claim 103 wherein said passivation agents are insulators.

105. A method according to claim 91 wherein said detecting is done using chronocoulometry.

REMARKS

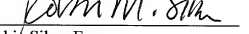
Claims 47-107 are pending in the application. Support for the added claims are provided in the following sections of the specification: support for claim 47 is found throughout the specification, for example on page 17, lines 15-28, page 18, page 66, lines 22-25, page 67, lines 1-16, page 70, lines 9-23 and page 85, lines 11-23; support for claims 48, 63, 80 and 92 is on page 70, lines 12-26 and page 71; support for claims 49, 64, 81, and 93 is on page 70, line 21-23 and page 50, line 27; support for claims 50-51, 65, 83, and 94 are on page 4, lines 17-24, page 5, lines 1-17, page 69, lines 5-14 and page 70, lines 9-23; support for claims 52, 66, 84, and 95 is on page 72, line 8-12 and page 73, line 5-10; support for claims 53-54, 67-67, 86-86, and 96-97 is found throughout the specification, for example on page 4, lines 12-24, page 5, lines 5-17, page 14, lines 6-13 and page 69, lines 5-27; support for claims 55, 69, 87, and 98 is found on page 73, lines 1-2; support for claims 56, 70, 88, and 99 are on page 14-23; support for claims 57, 71, 77, and 100 is found throughout the specification, particularly on page 85, line 10-12; support for claims 58, 72, 78 and 101 is on page 85, line 11-23; support for claims 59, 73, 79, and 102 is on page 25, lines 16-20, page 26 lines 8-10, page 47, lines 10-16 and lines 19-22f; support for claims 60, 74, 89, and 103 are found throughout the specification, particularly on page 45, lines 3-17; support for claims 61,75, 90, and 104 is on page 45, lines 18-25. support for claim 62 is found throughout the specification, particularly on page 41, line 7-9, page 44, lines 13-18, page 48, lines 5-8 and page 97, lines 13-15; support for claims 82 and 105 is on page 79, line 2;

support for claim 91 is on page 71, lines 25-26, page 72, lines 1-8, page 91, lines 21-26, page 92, lines 1-5; and page 95, lines 3-12.

The Applicants submit that the claims are in condition for allowance and an early notification of such is respectfully solicited.

Respectfully submitted

FLEHR HOHBACH TEST
ALBRITTON & HERBERT LLP



Robin Silva, Esq.
Reg. No. 38,304

Four Embarcadero Center
Suite 3400
San Francisco, CA 94111-4187
(415) 781-1989
(415) 398-3249

1065489.CO